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10/828,925	04/20/2004	Enrico Cappelleti	57637/1380	5906

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EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	**PAPER NUMBER**
1618	

NOTIFICATION DATE	DELIVERY MODE
10/09/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

klpatent@kramerlevin.com

Office Action Summary	Application No.	Applicant(s)	
	10/828,925	CAPPELLETI ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/31/07; 7/10/06; & 7/11/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51,53-59,61-70,82,84-86,88,90,108 and 109* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51,53-59,61-70,82,84-86,88,90,108 and 109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/23/06 & 7/29/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 7/10/06 wherein a substitute specification was submitted and some of the claims amended. The Examiner also acknowledges receipt of the amendment filed 7/11/05 wherein the specification was amended. In addition, the Examiner acknowledges receipt of the amendment filed 8/31/07 wherein claims 1-50, 52, 60, 71-81, 83, 87, 89, and 91-106 are canceled; claims 51, 53, 56, 58, 63, 64, 69, 84-86, 88, and 90 are amended; and claims 108 and 109 are added

Note: Claims 51, 53-59, 61-70, 82, 84-86, 88, 90, 108, and 109 are pending.

APPLICANT'S INVENTION

2. Applicant's invention is directed to compounds and uses thereof having the formula MNOPG wherein M is an optical label or a chelator/ligand optionally complexed to a radionuclide; N, O, and P are independently absent, an alpha amino acid, a non-alpha amino acid with a cyclic group, or a linking group; and G is a peptide target selected , from those listed by Applicant.

RESPONSE TO APPLICANT'S ELECTION

3. Applicant's election with traverse of Group VII filed 8/31/07 is acknowledged. The traversal is on the ground that a search for the claimed compounds themselves would necessarily uncover art relating to the methods of use. The rejection is withdrawn, but not because Applicant has suggested that the restriction should have

been based on the linker. The restriction is withdrawn because of the manner in which the claims have been amended, specifically, the claims have been amended to require compounds wherein the majority of the targeting peptides have a common core. However, Applicant is put on notice that the instant invention could very well have been restricted based on the fact that while some of the targeting peptides have a common core, some of them do not. Thus, one could properly restrict the various groups of peptides from one another. For example, SEQ ID No. 7, does not have the same core as those of SEQ ID No. 1.

It should be noted that the election of species requirement is maintained. Also, it is noted that Applicant elected the species wherein M is the chelator DO3A, the linker N-O-P comprises 4-aminobenzoic acid, and the targeting peptide G is QWAVGHLM-OH (SEQ ID No 1). The election of species requirement is still deemed proper and is therefore made FINAL.

Comments/Notes: Initially, Applicant's elected species was searched. No prior art was found to reject Applicant's elected species. Thus, the search was expanded over the full scope of claim 82 having the specific linker-peptide combination as set forth in the claim. However, it should be noted that the there are numerous double patenting rejections against independent claim 82. The search was then expanded to MNOPG wherein G is SEQ ID No 1, M is a chelator or optical label, and N and P are absent, a non-alpha amino acid with a cyclic group, or a linking group; or O is an alpha amino acid or a non-alpha amino acid with a cyclic group. The search was not further expanded because prior art was found which could be used to reject the claims.

DOUBLE PATENTING REJECTIONS

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 51, 53-59, 61-70, 82, 84-86, 88, and 90 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 7,226,577. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compounds and uses thereof wherein M = DO3A, the linker NOP comprises 4-aminobenzoic acid, and the targeting peptide is SEQ ID No 1 (elected species) and other GRP peptides in combination with NOP and various amino acids with cyclic groups (e.g., see patented claims 7 and 9). The claims differ in that those of the instant invention disclose specific GRP targeting peptides and the patented invention generally claims GRP peptides. Thus, the skilled practitioner would recognize that the patent and instant application discloses overlapping subject matter.

6. Claims 51, 53-59, 61-70, 82, 84-86, 88, and 90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-87 of copending Application No. 10/542,202. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compounds and uses thereof encompassed by the formula MNOPG. The claims differ in that in the instant invention specific GRP peptides are listed. However, it would be obvious to encompass the specific peptides of the instant invention since in some of the independent claims, the same peptides are listed. Hence, both applications disclose overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 51, 53-59, 61-70, 82, 84-86, 88, and 90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 11/165,721. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compounds and uses thereof encompassed by the formula MNOPG. The claims differ in that in the instant invention specific GRP peptides are listed. However, it would be obvious to encompass the specific peptides of the instant invention since in some of the independent claims, the same peptides are listed. Hence, both applications disclose overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 51, 53-59, 61-70, 82, 84-86, 88, and 90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-57 of copending Application No. 11/352,156. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compounds and uses thereof encompassed by the formula MNOPG. The claims differ in that in the instant invention specific GRP peptides are listed. However, it would be obvious to encompass the specific peptides of the instant

invention since in some of the independent claims, the same peptides are listed. Hence, both applications disclose overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 51, 53-59, 61-70, 82, 84-86, 88, and 90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 69-91 of copending Application No. 11/467,237. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compounds and uses thereof encompassed by the formula MNOPG. The claims differ in that in the instant invention specific GRP peptides are listed. However, it would be obvious to encompass the specific peptides of the instant invention since in some of the independent claims, the same peptides are listed. Hence, both applications disclose overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 51, 53-59, 61-70, 82, 84-86, 88, and 90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 69-91 of copending Application No. 11/467,301. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compounds and uses thereof encompassed by the formula

MNOPG. The claims differ in that in the instant invention specific GRP peptides are listed. However, it would be obvious to encompass the specific peptides of the instant invention since in some of the independent claims, the same peptides are listed. Hence, both applications disclose overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 51, 53-59, 61-70, 82, 84-86, 88, and 90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-17, 20-23, 26, 29, 30, 35, 36, 39-42, 50, 60, 61, 64-67, 74, 80, 81, and 84-87 of copending Application No. 10/566,112. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to compounds and uses thereof encompassed by the formula MNOPG. The claims differ in that in the instant invention specific GRP peptides are listed. However, it would be obvious to encompass the specific peptides of the instant invention since in some of the independent claims, the same peptides are listed. Hence, both applications disclose overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

112 SECOND PARAGRAPH REJECTIONS

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 51, 53, 55, 57, 59, 62, 64-67, 82, 84, 86, 90, 107, and 109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51, lines 7 and 10: The claim as written is ambiguous because it is unclear what 'other linking groups' Applicant is referring to which are compatible with the instant invention. It is respectfully suggested that Applicant replace 'other linking group' with 'linking group'.

Claim 53, line 12: In the chemical name, should '[3,21-**hi**]' be '[3,21-**bi**]'?

Claim 55, line 2: The claim is ambiguous because it is unclear what portion of the EHPG parent compound remains in the derivatives. In other words, what specific derivatives of EHPG are compatible with the instant invention?

Claim 57, line 2: The claim is ambiguous because it is unclear what portion of the benzo-DTPA parent compound remains in the derivatives. In other words, what specific derivatives of benzo-DTPA are compatible with the instant invention?

Claim 59, line 2: The claim is ambiguous because it is unclear what portion of the HBED parent compound remains in the derivatives. In other words, what specific derivatives of HBED are compatible with the instant invention?

Claim 62, lines 2-5: The claim is ambiguous because it is unclear what portion of the PDTA, TTHA, LICAM, and MECAM parent compounds remain in the derivatives. In

other words, what specific derivatives of PDTA, TTHA, LICAM, and MECAM are compatible with the instant invention?

Claim 64: The claim is ambiguous because it is unclear what specific compounds (e.g., chromophores, fluorophores, light absorbing compounds, light reflecting compounds, and bioluminescent molecules) are compatible with the instant invention. Is Applicant claiming that ALL chromophore, fluorophore, light absorbing compound, light reflecting compounds, and bioluminescent molecules are compatible with the instant invention?

Claims 65-67: What is being imaged? Is the claim 'A method of imaging a target area', 'A method of imaging a subject', etc. Please clarify in order that one may readily ascertain what is being claimed.

Claim 82, lines 5 and 7: The claim is ambiguous because it is unclear what 'other linking groups' are compatible with the instant invention. It is suggested that Applicant replace the phrase 'other linking group' with 'linking group'.

Claim 84: Did Applicant intend to write 'A method of phototherapy of a patient in need of therapy'?

Claim 86, line 2: The claim is ambiguous because it is unclear what 'other therapeutic agents' Applicant is intending to be compatible with the instant invention. Please clarify in order that one may readily ascertain what is being claimed.

Claim 90: Did Applicant intend to write 'P is 0' or 'P is absent'? This would be consistent with what is disclosed in the specification.

Claim 107: The claim is ambiguous because it is unclear whether Applicant intended to add additional text since the claim does not contain a period.

Claim 109: The claim as written is ambiguous because it appears to be missing some text and three is no period in the claim.

103 REJECTION

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 51, 54-62, 64-70, 88, and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman et al (US Patent No. 7,147,838) in view of both Hu et al (Nuclear Medicine and Biology, 2002. Vol. 29, pp. 423-430) and Achilefu et al (J. Med. Chem. 2002, Vol. 454, pp. 2003-2015).

Hoffman et al disclose gastrin receptor peptide conjugates useful as therapeutic or diagnostic radiopharmaceuticals. The conjugates may be complexed to a metal directly or indirectly using a spacer/linker group (see entire document, especially, abstract). Figure 2, discloses a radiometal chelate, a spacer group which includes the amino acid glutamine (represented by the symbol Q). In particular, the compounds of Hoffman et al have the general structure, X-Y-B wherein X is a group capable of complexing a metal (i.e., a radiometal), Y is a covalent bond or a spacer group; and B is a bombesin agonist binding compound. Hoffman et al disclose that its spacer group

may include a peptide having one or more amino acid residues (column 5, lines 30-49; columns 5-6, bridging paragraph). The metal complexing chelator may includes monodentate and polydentate chelators (column 6, lines 29-53). The bombesin agonist includes, as demonstrated in the art, requires residues 8-14 (columns 6-7, bridging paragraph). When the conjugates are labeled, they may be used to treat and/or detect cancers (column 9, lines 26-31). Thus, both Hoffman and Applicant disclose compounds encompassed by Applicant's formula MNOPG. However, while Hoffman et al disclose that bombesin (8-14) is a preferred peptide (note that Hoffman et al's preferred peptide differs by one amino acid residue, glutamine (Q), from that of Applicant's SEQ No. 1), it does not disclose that bombesin (7-14) in combination with a spacer and metal moiety.

Hu et al disclose Pm-149 DOTA bombesin analogs. In addition, Hu et al disclose Sm-153 and Lu-177 labeled DO3A bombesin analogs wherein the bombesin peptide has residues 7-14 as set forth in the instant invention (see entire document, especially, abstract; and page 424, Figure 2).

Achilefu et al disclose fluorescein and carbocyanine peptide-based metal binding/optical contrast agents. The bombesin analogues may have metal binding moieties such as DTPA, FITC, and DOTA (see entire document, especially, abstract; page 2006, Tables 3 and 4; page 2009, Figure 6).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to generate compounds and uses thereof wherein the compound encompass the formula MNOPG as set forth in the instant invention because Hoffman

et al discloses gastrin receptor peptide conjugates useful for therapeutic or diagnostic purposes comprising a metal attached to a moiety (i.e., chelator/ligand) that may conjugated to a bombesin agonist binding moiety by a spacer (linker) group. It would be obvious to the skilled artisan to use various spacers which as disclosed by Hoffman et al can include peptides which Hoffman et al has defined as having one or more amino acid residues. Furthermore, it would be obvious to the skilled artisan to include the amino acid residue glutamine (represented by the symbol Q) in combination with the bombesin 8-14 binding peptide of Hoffman et al because in Figure 1 of Hoffman et al, the amino acid Q is attached to the 8-14 bombesin binding region of the peptide. Also, since Hoffman et al disclose that any amino acid residue(s) may be used to link the metal moiety to the peptide, the skilled artisan would recognize that in the listing of non-modified amino acid residues, the amino acid residues histidine, phenylalanine, tyrosine, and tryptophan all meet the limitation of a non-alpha amino acid having a cyclic group.

It would be obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Hoffman et al using the teachings of Achilefu et al and Hu et al and generate various compounds of formula MNOPG wherein the M moiety varies because both Achilefu et al and Hu et al disclose that the metal moiety attached to the bombesin peptide may be FITC, DTPA, DOTA, or DO3A. Thus, it would be obvious to alter the metal moiety. Since the references disclose bombesin in combination with a metal binding moiety, the references may be considered to be within the same field of endeavor. Thus, the reference teachings are combinable.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D. L. Jones
Primary Examiner
Art Unit 1618

September 24, 2007